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Short Communication

Potential risk of inguinal hernia in complete androgen insensitivity syndrome

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Highlights

- Sharing IH risk can minimize parental anxiety when IH occurs.
- Sharing IH risk is beneficial for all CAIS patients without a history of IH.
- Parents' condition and understanding may determine when to discuss IH risk.

Key words: androgen insensitivity syndrome, complete, inguinal hernia

Introduction

Complete androgen insensitivity syndrome (CAIS) presents as female external genitalia despite elevated serum testosterone levels and an XY karyotype, because of compromised androgen action owing to androgen receptor (AR) defects (1). Sporadic CAIS is usually diagnosed based on inguinal hernia (IH) or primary amenorrhea (1, 2). When CAIS is diagnosed in neonates or infants before the development of IH, it is unknown whether the potential risk of IH should be addressed during genetic counseling. Here, we report the case of an infant with CAIS who developed IH during follow-up, conveying the importance of sharing the potential risk of IH with parents soon after the diagnosis of CAIS.

Case Report

The patient was the first child of a non-consanguineous Japanese couple. The mother had a history of ventricular septal defects and idiopathic thrombocytopenic purpura. Non-invasive prenatal genetic testing upon the parents' requests revealed a Y chromosome component. At birth, the infant's external genitalia were female and normal, and the sex of the baby was assigned as female. Chromosome analysis of the peripheral blood showed 46,XY, indicating differences in sex development. The baby was referred to our hospital at 4 months of age. The physical examination results were as follows: clitoral width, 6 mm; anogenital ratio, 0.3; and urethral meatus and vaginal opening, separate at the perineum. Endocrinological examinations showed that serum anti-Mullerian hormone levels were high (461 ng/mL, reference range in males at the age of 4–12 months: 27.4–197 ng/mL). In addition, serum testosterone levels showed an increase on the human chorionic gonadotrophin loading test (basal 2.38 ng/mL, peak 27.2 ng/mL). Abdominal ultrasonography and magnetic resonance imaging revealed no uterus or ovaries, but testes-like masses almost 2 cm in diameter were noted in the inguinal canals on both sides. After obtaining informed consent from the parents, genomic

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DNA was extracted from peripheral blood samples. Sanger sequencing revealed a previously reported *AR* gene pathogenic variant, *AR* (NM_000044.6) c.2599G>A, p.Val867Met (3). Thus, the patient was diagnosed with CAIS. We provided genetic counseling and shared the pathogenesis of CAIS. Next, we discussed management for the testes with her parents as follows: i) estradiol converted from testosterone secreted by the testes would initiate and maintain spontaneous puberty as a female, except for menstruation; ii) CAIS patients have an increased risk for the occurrence of gonadal tumors from adolescence (4, 5); and iii) gonadectomy is recommended after puberty. After repeated counseling sessions with the parents, they decided to consult with us about gonadectomy in the patient after puberty. However, we did not share the risk of future IH.

At nine months of age, the mother found a bulge in the patient's right inguinal region when crying. The mother searched the internet for a possible cause of the bulge and came up with the possibility of IH by herself. The mother brought the patient for an emergency visit. Our patient was diagnosed with IH and underwent a manual reduction. A few days later, the patient revisited the emergency department due to IH recurrence. Subsequently, surgical repair of the IH was performed. The parents inquired whether the testes could be resected simultaneously during surgical IH repair by combining the two procedures into one operation. We repeatedly discussed the advantages and disadvantages of combined gonadectomy during surgical IH repair until the operation: the number of surgeries would be reduced, but puberty would not initiate spontaneously. Finally, the parents decided for gonadectomy to be postponed until after puberty as initially planned. Therefore, only IH repair surgery was performed. Operative findings showed that the bilateral peritoneal sheaths were patent, and the patient was diagnosed with bilateral IH.

Ethical statement

This study complies with all the relevant national regulations and institutional policies, is in accordance with the tenets of the Helsinki Declaration, and was approved by the Institutional Review Board at Keio University School of Medicine (Institutional Review Board number 20170130). Written informed consent was obtained from the patient's parents.

Discussion

We report a case of an infant with CAIS who developed bilateral IH during the follow-up period. When IH occurred, the mother became very anxious, searched for symptoms by herself, and brought the patient for an emergency visit twice. The emotional burden on the parents was significant because of the limited time window for deciding whether gonadectomy should be performed simultaneously during IH repair surgery. If we had previously shared the potential risk of developing IH and instructed the parents on how to observe and treat it, the parents might have been less anxious when they found a bulge in the inguinal region in the patient.

The prevalence of IH as a complication of CAIS remains unknown. A previous study showed that 28 of 29 patients with CAIS developed IH (6). Another study showed that 48 of 72 patients with CAIS were clinically diagnosed with IH (7). Thus, we believe that the frequency of IH is sufficiently high to consider the potential risk of IH in all infants with CAIS.

The risk of future IH must be carefully shared with parents. The mental condition of parents should be considered when discussing future IH risks. In addition, to improve the parents' knowledge of IH, we must explain the pathogenesis of CAIS. If these conditions are not met, sharing IH risk information could lead to further anxiety.

In conclusion, we believe we should share the potential risk of IH in infants with CAIS with their parents in advance, thereby minimizing their anxiety if and when IH were to occur. The appropriate time at which future IH risk should be addressed depends on the parents' psychological condition and understanding of CAIS pathogenesis.

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